



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.				
10/537,711	11/28/2005	Shiping Xu	U 015799-6	6874				
140 LADAS & PARRY LLP 26 WEST 61ST STREET NEW YORK, NY 10023	7590 11/09/2010		<table border="1"><tr><td>EXAMINER</td></tr><tr><td>LEESER, ERICH A</td></tr></table>		EXAMINER	LEESER, ERICH A		
EXAMINER								
LEESER, ERICH A								
			<table border="1"><tr><td>ART UNIT</td><td>PAPER NUMBER</td></tr><tr><td>1624</td><td></td></tr></table>	ART UNIT	PAPER NUMBER	1624		
ART UNIT	PAPER NUMBER							
1624								
			<table border="1"><tr><td>NOTIFICATION DATE</td><td>DELIVERY MODE</td></tr><tr><td>11/09/2010</td><td>ELECTRONIC</td></tr></table>	NOTIFICATION DATE	DELIVERY MODE	11/09/2010	ELECTRONIC	
NOTIFICATION DATE	DELIVERY MODE							
11/09/2010	ELECTRONIC							

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

nyuspatactions@ladas.com

### Office Action Summary

**Application No.**

10/537,711

**Applicant(s)**

SHIPPING

**Examiner**

Erich A. Leeser

**Art Unit**

1624

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 September 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 2, 4, 5, 7, 9-11, 19-25 and 27 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-2, 4-5, 7, 9-11, 19-25, and 27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This action is in response to Applicant's submission dated September 30, 2010, in which Applicant cancelled claims 3, 6, 8, 12-18, and 26, and amended claims 1-2 and 5.

#### ***Claim Rejections - 35 USC § 112***

Examine previously rejected claims 19-20, 22, and 25 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not enable the instant compounds to inhibit transforming growth factor  $\beta$ 1 or angiotensin II (AngII) receptor converting enzyme; treat a chronic renal disorder; cardio-cerebrovascular disease, including hypertension, cerebral embolism, myocardial infarction, cerebrovascular accidents, or stroke; non-insulin dependent diabetes; or a tumor or pre-cancerous lesion using an effective amount of a compound corresponding of formula (I) or enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Applicant argues that as "can be seen from the experimental Example 3 that begins on page 59 of the specification, in particular table 5B and D, it is clear that the present compounds do have the effect of decreasing TGF $\beta$ 1 and Ang II serum level, and thus illustrate the activity of inhibiting TGF $\beta$ 1 and Ang II receptor converting enzyme.

Examiner does not find this argument persuasive because looking at the two tables that Applicant has pointed out, the dose of Benazepril was 4 mg/kg and Losartan was 10 mg/kg, while Compound 149 was tested at doses of 7.5, 15, and 30 mg/kg. Not only are the doses inconsistent between the test and the control groups, but at the lowest dose for Compound 149 the percentage change included both increase and decrease results.

As such, Examiner maintains this rejection with regards to claims 19-20.

***Claim Rejections - 35 USC § 112***

Examiner previously rejected claims 1-7, 9-11, and 19-27 under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for making hydrates of the claimed invention. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Because the specification in fact includes hydrates as pointed out by Applicant, Examiner withdraws this rejection.

***Claim Rejections - 35 USC § 102***

Examiner previously rejected claims 1-3, 10-11 and 27 under 35 USC 102(b) as being anticipated by El-Kerdawy, et al., *Application of the Knoevenagel Condensation to 4-acetamidophenazone Derivatives*, Indian J. of Chemistry, Section B: Organic Chem. Including Medicinal Chem., 26B(12), 1189-91 (1987); claims 1, 4, 10-11 and 27 under 35 USC 102(e) as being anticipated by Levy, et al., U.S. Patent Publication No. 2003/0229065; claims 1-2 and 4 under 35 USC 102(b) as being anticipated by Bylov, et al., *Synthesis and Anti-inflammatory Activity of N-substituted 2-oxo-2H-1-benzopyran-3-carboxyamides and Their 2-iminoanalogues*, Eur. J. Med. Chem. 34, 997-1001 (1999); claims 1-2, 4, 10-11 and 27 under 35 USC 102(b) as being anticipated by Ogiso, et al., JP 06145164; claims 1-2, 4, 10-11 and 27 under 35 USC 102(b) as being anticipated by Reusser, et al., WO 89/07939.

First, Applicant argues that the "pyrazole-derived substituents are deleted from Claim 1, thus the compounds of Claim 1 and the claims dependent thereon are not anticipated by El-Kerdawy." Examiner agrees and withdraws the rejection with regards to El-Kerdawy.

Next, Applicant argues that the "definition of R<sub>7</sub> is amended to exclude hydrogen." Examiner does not find this argument persuasive because in claim 1 and its dependent claims, R<sub>7</sub> still includes hydrogen in its definition. As such, Examiner maintains this rejection with regards to the remaining references and claims 1-2, 4, 10-11 and 27.

#### ***Claim Rejections - 35 USC § 103***

Examiner previously rejected claims 1-3, 10-11 and 27 under 35 U.S.C. 103(a) as being unpatentable over El-Kerdawy, et al., *Application of the Knoevenagel Condensation to 4-acetamidophenazone Derivatives*, Indian J. of Chemistry, Section B: Organic Chem. Including Medicinal Chem., 26B(12), 1189-91 (1987); claims 1-4, 10-11 and 27 under 35 U.S.C. 103(a) as being unpatentable over Ukhov, et al., *Synthesis and Antimicrobial Activity of 2-Iminocoumarin-3-carboxylic acid amides*, Pharmaceutical Chemistry Journal, Vol. 35, No. 7 (2001); and claims 1-4 under 35 U.S.C. 103(a) as being unpatentable over Bylov, et al., *Synthesis and Anti-inflammatory Activity of N-substituted 2-oxo-2H-1-benzopyran-3-carboxyamides and Their 2-iminoanalogues*, Eur. J. Med. Chem. 34, 997-1001 (1999).

Applicant argues that since none of the references above disclose "a compound with substitution in the 7th-position, the claimed compounds are inventive" over them. Examiner does not find this argument persuasive because not only does it not address the issues raised in the Office action, but the 7th-position of the instant compounds can be hydrogen and therefore

substitution is not required at this position. As such, Examiner maintains this rejection with regards to claims 1-2, 10-11 and 27.

*New Grounds of Rejection Necessitated by Amendment*

*Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4-5, 7, 9-11, 19-25 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i) In claim 1, the definition of R<sub>7</sub> is as follows:

R<sub>7</sub> is selected from the group consisting of H, hydroxyl, C<sub>1</sub>-C<sub>4</sub> alkyl and ~~[[or]]~~ alkoxy, carboxyalkylenoxy, and OCH<sub>2</sub>CO~~NR<sub>11</sub>~~ where R<sub>11</sub> is selected from the group consisting of ~~un-substituted, mono- or multi-~~ substituted phenyl wherein the substituent is selected from the group consisting of hydroxyl, OCH<sub>3</sub>, CF<sub>3</sub>, CO<sub>2</sub>H, CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>, and NO<sub>2</sub>.

It is improper for "and" to be introduced between the alkyl and alkoxy choices in place of ~~[[or]]~~ because MPEP 2173.05(h) provides that proper Markush language is "selected from the group consisting of A, B, C and D". The instant recitation has "A, B, C **and** D, E **and** ... F", which is not proper for this reason. Correction is required.

ii) Next, claim 1 contains the partial group "OCH" and the rest of R<sub>7</sub> has been deleted by a line through. Two of the electrons of the carbon atom are unaccounted for and so OCH is

indefinite. It is unknown if this moiety is monovalent or divalent. Correction is required.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Erich A. Leaser whose telephone number is 571-272-9932. The Examiner can normally be reached Monday through Friday from 8:30 to 6:00 EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) toll-free at 866-217-9197. If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

**/Erich A. Leeser/**  
*Patent Examiner*, Art Unit 1624  
United States Patent and Trademark Office  
400 Dulany Street, Remsen 5C11  
Alexandria, VA 22314-5774  
Tel. No.: (571) 272-9932

**/James O. Wilson/**  
*Supervisory Patent Examiner*, Art Unit 1624  
United States Patent and Trademark Office  
400 Dulany Street, Remsen 5A11  
Alexandria, VA 22314-5774  
Tel. No.: (571) 272-0661